bupivacaine, however, is a "fast-in, slow-out" agent. As a result of the slow recovery with the use of bupivacaine, a substantial frequency-dependent block accumulates at heart rates between 60 and 150 beats per minute (slow recovery from block during diastole). Bupivacaine is therefore more cardiotoxic than lidocaine at clinically equivalent local anesthetic concentrations; bupivacaine is potentially cardiotoxic when a large dose (probably 1 mg per kg of body weight or greater) is given intravascularly.

In August 1984, with an increasing number of reported deaths related to accidental intravascular bupivacaine injection, mostly among the obstetric population, the Food and Drug Administration issued urgent new recommendations about bupivacaine, stating that the 0.75% concentration is no longer recommended for obstetric anesthesia. The reason for the increased incidence of cardiotoxic reactions to bupivacaine in pregnancy is not clear. It may be due to the more frequent use of bupivacaine for obstetric epidural blocks or possibly that the physiologic changes during pregnancy make a woman more susceptible to such reactions, or more difficult to resuscitate, than a nonpregnant woman.

Despite its potential cardiotoxicity, bupivacaine remains a very useful agent for regional anesthesia, with a longer duration of action than lidocaine and, in lower concentrations, the ability to produce a high-quality analgesic block with minimal motor block. With careful administration and using meticulous techniques of test dosing and slow administration of a dose in fractional amounts, bupivacaine can be used effectively and safely. It is apparent, however, that great caution must be exercised to prevent an accidental intravascular injection of a large dose of bupivacaine, whatever the concentration.

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REFERENCES

Albright GA: Cardiac arrest following regional anesthesia with etidocaine or bupivacaine (Editorial). Anesthesiology 1979 Oct; 51:285-287

Clarkson CW, Hondeghem LM: Mechanism for bupivacaine depression of cardiac conduction: Fast block of sodium channels during the action potential with slow recovery from block during diastole. Anesthesiology 1985 Apr; 62:396-405

Kotelko DM, Shnider SM, Dailey PA, et al: Bupivacaine-induced cardiac arrhythmias in sheep. Anesthesiology 1984 Jan; 60:10-18

Rosen MA, Thigpen JW, Shnider SM, et al: Bupivacaine-induced cardiotoxicity in hypoxic and acidotic sheep. Anesth Analg 1985; 64:1089-1096

Hypokalemia and Potassium Administration in the Perioperative Period

PERIOPERATIVE HYPOKALEMIA has given anesthesiologists cause for concern due to the accepted relationship between low serum potassium levels and cardiac dysrhythmias. Two practices resulting from this concern have recently been questioned: automatic postponement of elective surgical procedures when a serum potassium level is below arbitrarily chosen levels, resulting in inconvenience to the patient and the surgical team and a pronounced increase in the cost of hospital care; second, aggressive intravenous replacement of potassium that in itself can precipitate serious morbidity and mortality.

Serum potassium levels reveal little information about the total body exchangeable potassium (representing 0.4% of the total body potassium). If a serum potassium concentration of 4.0 mEq per liter is considered normal, a potassium level of 3.0 mEq per liter reflects a 25% deficit of total body potassium. In a 70-kg adult, this represents 1,100 mEq of potassium, too great a deficit to replace rapidly with safety. Acute hypokalemia can be seen during anesthesia; for example, a decrease in a serum potassium level of 1 mEq per liter can result from hyperventilation that reduces the arterial carbon dioxide pressure from 45 torr to 25 torr, resulting in no loss of total body potassium and a 12-mEq transfer from the extracellular to the intracellular compartment of potassium ions. Replacement in this situation is unnecessary and carries the risk of a dangerously high serum potassium level being attained.

Studies by Vitez and colleagues of patients with chronic hypokalemia and by Allard and Cheek of patients with acute hypokalemia seen intraoperativelay both suggest that the dangers of hypokalemia in the perioperative period may have been overstated and may be less than that of iatrogenic hyperkalemia from overadministration or too rapid an administration of potassium.

The commonly accepted potassium levels for an elective operation (3.0 mEq per liter for chronic hypokalemia and 3.5 mEq per liter for hypokalemia and digitalis therapy) are arbitrary generalizations that the study of Vitez and associates would suggest are too high to routinely cancel surgical procedures. The interpretation of a single potassium level should be judged individually in light of the clinical situation within which it is found, and electrocardiographic evidence of hypokalemia should be elicited. If potassium is to be administered in a patient with chronic hypokalemia, it should ideally be given before the admission of the patient for an operation. If hypokalemic-related cardiac dysrhythmias occur and intravenous repletion of potassium is considered necessary, it should be administered in dilute solution through a central line at a maximum rate of 0.5 mEq per kg per hour with continuous electrocardiographic monitoring.

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REFERENCES

Allard MW, Cheek DBC: Omission of supplementary potassium perioperatively in cardiac surgery (Abstr). Anesth Analg 1985 Feb; 64:189

McGovern B: Hypokalemia and cardiac arrhythmias. Anesthesiology 1985 Aug; 63:127-129

Vitez TS, Soper LE, Wong KC, et al: Chronic hypokalemia and intraoperative dysrhythmias. Anesthesiology 1985; 63:133-135

Malignant Hyperthermia Update

IN THE EARLY 1970s, malignant hyperthermia was the leading cause of anesthetic deaths, with an estimated mortality rate of 65% to 80%. By the mid-1980s mortality rates have dropped to below 5%. This dramatic change in statistics can be attributed to several factors: an awareness by the medical and lay community, with the increased detection of persons who might be susceptible to malignant hyperthermia; the early detection and treatment of malignant hyperthermia by anesthesiologists, and the availability (1979) of injectable dantrolene sodium, a drug that effectively reverses a malignant hyperthermia crisis.

Typically the syndrome is manifested by sinus tachycardia, a rising blood pressure and tachypnea. The skin becomes mottled—cyanotic with patches of bright red flushing. Rigor mortis-like stiffening of masseter or all skeletal muscles may develop. The temperature increase that results from the hypermetabolic condition in skeletal muscle occurs relatively late. In fulminant cases the syndrome may progress in as few as 20 minutes to severe acidosis, a rise in the end-tidal carbon dioxide, shock and ventricular fibrillation with only a modest fever.

Laboratory findings of metabolic and respiratory acidosis may be detected before an increase in temperature. Arterial oxygenation remains adequate despite pronounced cyanosis. After an initial rise in the serum potassium levels to between 6 and 14 mEq per liter, hypokalemia may develop as a result of redistribution and urinary excretion. Serum creatine phosphokinase (CPK) levels start rising as soon as a crisis begins but do not reach peak values for 12 to 48 hours.

The recommended treatment of acute malignant hyperthermia is to discontinue administration of the triggering drugs, hyperventilate with 100% oxygen and administer dantrolene, 2.5 mg per kg, intravenously as quickly as possible. If rigidity, acidosis and tachycardia are not reversed in a few minutes, additional dantrolene (up to 10 mg per kg) should be given. Acidosis correction may require giving sodium bicarbonate, 1 or 2 mEq per kg. Frequent determinations of arterial blood gases and electrolytes, glucose and serum CPK measurements will assist management. Dantrolene therapy should be continued at 2.5 mg per kg every six hours until the crisis fully resolves. The urine output should be monitored because myoglobinuria may be followed by acute tubular necrosis. If the clinical and laboratory findings return to normal with the use of dantrolene, cooling measures may not be needed.

Early recognition is critical in treating a malignant hyperthermia crisis. No patient receiving less than ten minutes of anesthesia has died. Conversely, all patients for whom treatment was delayed more than two hours have succumbed.

Malignant hyperthermia is a familial disease, but its genetics remain unclear. Originally thought to have an autosomal dominant inheritance, the actual pattern appears more complex. In a personal or familial anesthetic history, items such as unexplained cardiac problems, fever, muscle rigidity and prolonged recovery from anesthesia should not be ignored.

The reported incidence of malignant hyperthermia is approximately 1 in 12,000 anesthesia inductions in children and 1 in 40,000 anesthesia inductions in adults. This discrepancy is not understood. Thiopental sodium, commonly used for adult inductions, has been shown to delay the onset and severity of the syndrome, but this drug is less frequently used in pediatric anesthesia.

The most reliable test for a susceptibility to malignant hyperthermia is a contracture test done on a fresh biopsy specimen of muscle. The muscle segments are removed under local anesthesia or during an indicated elective general anesthetic and are immediately suspended in an oxygenated bath. Diagnosis is established by observing the contractions of the muscle in response to caffeine and halothane, which have little effect on normal muscle. This test is not routine and is done in only a few centers. A recently developed test using calcium uptake in thin, frozen muscle slices, although not fully evaluated, suggests that the increase of susceptibility may be greater than previously reported.

An elective surgical procedure is not contraindicated in patients known to be susceptible. Regional anesthesia is preferred, although care should be taken to avoid unnecessary stress. General anesthesia can be done safely with a nitrous oxide-narcotic technique augmented by nondepolarizing muscle relaxants as needed. Some physicians prophylactically administer dantrolene intravenously or by mouth, whereas others believe it is unnecessary. In a crisis, intravenously given dantrolene is effective within one or two circulation times.

Patients who may have had a hyperthermic crisis and close relatives with either a myopathy or increased CPK activity must be considered susceptible until a biopsy proves otherwise. They should wear a Medic-Alert tag that reads, "Malignant Hyperthermia—No potent inhalation anesthetics or succinylcholine." They should be referred to the Malignant Hyperthermia Association of the United States, PO Box 3231, Darien, CT 06820, telephone (203) 655-3007. This organization publishes an informational quarterly designed for the lay public. The association maintains a 24-hour physician referral service to assist with both crises and elective management.

The status of malignant hyperthermia in dental anesthesia has raised considerable controversy. Any clinic administering general anesthesia to dental patients must be adequately equipped to handle a crisis. This includes an immediately available supply (at least 36 ampuls) of dantrolene. In the 1970s there were reports that the amide local anesthetics, such as lidocaine, were capable of producing a crisis. Recent statistical analysis of many dental anesthetics has not supported this premise. The small amount of amide local anesthetics used in most dental cases is probably safe. If a patient is known to be susceptible to malignant hyperthermia, the procedure should be done in a fully equipped operating room.

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REFERENCES

Adragna MG: Medical protocol by habit—The avoidance of amide local anesthetics in malignant hyperthermia susceptible patients. Anesthesia 1985 Jan; 62:99-100

Britt BA: Malignant hyperthermia, *In* Orkin FK, Cooperman LH (Eds): Complications in Anesthesiology. Philadelphia, JB Lippincott, 1983, pp 291-313

Gallamore SE (Ed): The Communicator, vol 1-4. Darien, Conn, Malignant Hyperthermia Association of the United States, 1982-1985

The Choice of Anesthesia in Myocardial Ischemia

THE CHOICE of anesthetic agent for a patient with myocardial ischemia is controversial. Slogoff and Keats showed that the occurrence of intraoperative ischemia during coronary artery bypass grafting resulted in a threefold increased risk of postoperative infarction.

The choice of an anesthetic depends on an understanding of its effects on the major determinants of myocardial oxygen consumption: contractility, wall tension and heart rate as well as any direct effects on the coronary circulation. Clinical studies generally have relied on indirect hemodynamic measures of myocardial oxygen balance and electrocardiographic evidence of ischemia. In several studies, global myocardial blood flow and lactate metabolism have been estimated using coronary sinus catheterization. Interpreting these studies is difficult due to the inability to assess regional ischemic changes accurately, although the intraoperative use of two-dimensional transesophageal echocardiography will be helpful in future studies. Cardiac work clearly should not be